

What is claimed is:

1. A method of obtaining structural characteristic information from molecular specimens present in a solvent comprising the steps of:
 - providing a substantially planar solvophobic sample support having optically smooth substrate with a top surface covered by a solvophobic coating,
 - applying a droplet of a specimen-containing solvent to the sample support surface,
 - evaporating the solvent from the droplet at a rate permitting formation of a ring-like region of enhanced specimen deposit on the sample support surface,
 - irradiating a portion of the region of enhanced specimen deposit with a beam directed by an optical system aligned substantially normal to the sample support surface,
 - collecting radiation from the irradiated portion, and
 - detecting a selected spectra segment of the collected radiation.
2. The method of claim 1 wherein the providing step comprises the step of covering a metallic surface having a roughness of less than one-tenth the wavelength of the irradiating beam with the solvophobic enhancing layer to a thickness of about one-quarter the wavelength of the irradiating beam.
3. The method of claim 2 further comprising the step of forming the solvophobic enhancing layer to a thickness of between about 10 nm and about 300 nm from a fluorinated polymer, fluorinated hydrocarbon, or thiol derivative of a hydrocarbon.
4. The method of claim 3 further comprising the steps of diluting the material forming the solvophobic enhancing layer with a solvent and applying the diluted material to the metallic surface while the substrate is spinning.
5. The method of claim 1 wherein the applying step includes the step of forming the specimen-containing solvent into a droplet having a volume of

between about 10 nl and about 10 μ l, the specimen being present in the droplet at less than about 100 μ M concentration.

6. The method of claim 5 wherein the applying step includes the steps of chromatographically concentrating the specimen to a selected fraction of a flow of liquid and depositing a droplet from the selected fraction onto the sample support surface.

7. The method of claim 6 further comprising the steps of arranging an array of droplets on the sample support surface and comparing the selected spectra segments of the droplets forming the array.

8. The method of claim 7 further comprising the step of forming the array of droplets from specimens collected from a single source at different times to provide a history of the single source.

9. The method of any of claims 5-8 comprising the step of micro printing the droplets onto the sample support surface.

10. The method of claim 1 further comprising the steps of situating the sample support within an environmental control chamber and controlling the vapor pressure of the solvent within the chamber.

11. The method of claim 1 further comprising the step of focusing the irradiating beam onto a spot having a diameter of between about 1 μ m and 100 μ m, and positioning the irradiating beam within about 100 μ m of an edge of said specimen deposit.

12. The method of claim 1 further comprising the steps of forming the irradiating beam with an excitation laser having a output power of less than 100 mWatts and integrating the collected radiation for a time of between 5 seconds and 500 seconds.

13. The method of claim 1 further comprising the steps of forming the irradiating beam with an excitation laser having an output power of between about 1 and 100 Watts and integrating the collected radiation for a time of between about 0.01 and 1 seconds.

14. The method of claim 12 or 13 further comprising the step of collecting the collected radiation back through a portion of the optical system delivering the excitation laser output.
15. The method of claim 14 further comprising the step of processing the detected spectra using a Savistky-Golay second derivative algorithm.
16. The method of claim 14 further comprising the step of classifying the processed spectra with a partial least square discriminant program.
17. The method of claim 16 further comprising the step of plotting the classified spectra as a pseudo probability.
18. The method of claim 15 further comprising the step of normalizing the output of the second derivative algorithm.
19. The method of claim 18 further comprising the step of subtracting the normalized spectral outputs of two specimens to detect any spectral differences.
20. The method of claim 1 wherein the detecting step comprises the steps of analyzing the collected radiation in the IR range followed by analyzing the normal Raman spectra from an identical irradiated portion of the specimen.
21. The method of claim 20 further comprising the step of subjecting the identical irradiated portion of the specimen to a MALDI TOF MS evaluation.
22. A molecular sample support to facilitate exposure of a specimen present in a solvent to radiation of a selected wavelength, the holder comprising a substantially planar substrate, a surface on the substrate having a roughness of less than about one-tenth the wavelength of the radiation, and a solvophobic enhancement layer of less than about one-quarter the wavelength of the radiation covering the substrate surface.
23. The molecular sample support of claim 22 wherein the solvophobic enhancement layer consists essentially of a fluorinated polymer, a fluorinated hydrocarbon, or a thiol derivative of a hydrocarbon.

24. The molecular sample support of claim 22 wherein the solvophobic enhancement layer consists essentially of polytetrafluoroethylene deposited on the substrate while the substrate is spinning.
25. The molecular sample support of claim 22 wherein the substrate comprises a layer of metal selected from gold, stainless steel, silver, platinum, titanium, and aluminum, and alloys of these metals.
26. The molecular sample support of claim 25 further comprising a glass surface supporting the layer of metal.
26. The molecular sample support of claim 22 wherein the substrate comprises a layer of quartz, germanium, gallium arsenide, or zinc sulfide.
27. The molecular sample support of claim 22 wherein the substrate comprises a layer of a polymeric material selected from polyethylene, polypropylene, polycarbonate, polyacrylate, polymethacrylate, and polystyrene.
28. A method of reducing interference in Raman spectra taken from a specimen containing an analyte and a contaminant comprising the steps of:
- forming a solution of the specimen in a solvent,
 - providing a substantially planar solvophobic sample support having optically smooth substrate with a top surface covered by a solvophobic coating,
 - applying a droplet of a specimen-containing solvent to the sample support surface,
 - evaporating the solvent from the droplet at a rate permitting formation of a ring-like region of enhanced specimen deposit on the sample support surface,
 - irradiating a portion of the region of enhanced specimen deposit with a beam directed by an optical system aligned substantially normal to the sample support surface,
 - collecting radiation from the irradiated portion, and
 - detecting a selected spectral segment of the collected radiation.

29. The method of claim 28 wherein the contaminant is one generating fluorescence interference and the method further comprises the step of photo-bleaching the portion of the region of enhanced specimen deposit by pre-exposing the portion of the region to a beam from a Raman excitation laser.
30. The method of claim 28 wherein the contaminant is a buffer and the collecting step is from a portion of the ring-like region so as to minimize the spectral interference of the buffer.
31. The method of claim 1 or 28 further comprising the step of comparing the detected spectral segment to other similarly acquired spectral segments of known compositions.
32. The method of claim 31 wherein the comparing step includes the steps of calculating the second derivative of each spectral curve, and classifying the derivative curves into clusters of similar specimen composition.
33. The method of claim 31 wherein the comparing step includes assigning commonly observed spectral features to known structural features of the known compositions and looking for such commonly observed spectral features in spectra of at least partially unknown compositions to detect physiological or conformational structure similarities therein.
34. The method of claim 33 further comprising the step of quantifying the fractional portion of the sample population exhibiting a given physiological or conformational structure.
35. A method of obtaining structural characteristic information from molecular specimens present in a solvent comprising the steps of:
- providing a substantially planar solvophobic sample support having optically smooth substrate with a top surface covered by a solvophobic coating,
 - micro-printing an array of droplets of a specimen-containing solvent to the sample support surface,

evaporating the solvent from each droplet at a rate permitting formation of a ring-like region of enhanced specimen deposit on the sample support surface at each droplet location,

scanning the ring-like regions to locate hot spots of significant specimen deposit, and

collecting radiation from the hot spots to detect a selected spectra segment of the collected radiation.

36. The method of claim 35 wherein the scanning step is performed using FTIR.

37. The method of claim 36 wherein the radiation collected is Raman scattering.

38 The method of claim 35 wherein the micro-printing step is repeated to co-deposit additional droplets on each ring-like deposit in the array.

39. The method of claim 38 wherein the evaporating step is repeated after each repetition of the micro-printing step.